Non-stick Coating of a Protein Found in Semen Reduces HIV Infection of Immune Cells

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A non-stick coating for a substance found in semen dramatically lowers the rate of infection of immune cells by HIV a new study has found.

The new material, developed by chemists at the University of California, San Diego, is a potential ingredient for microbicides designed to reduce transmission of HIV, a team from UCSD and the University of Rochester Medical Center reports in a forthcoming issue of the *Journal of Biological Chemistry*.

The coating clings to fibrous strings and mats of protein called SEVI-for semen-derived enhancer of viral infection-which was first discovered just three years ago. SEVI seems to attract the virus and deposit it onto the surface of T-cells, components of the immune system that are the primary target of HIV infection, and may play an important role in sexual transmission of HIV.

Like the fibrous strings that bind senile plaques associated with Alzheimer's disease, SEVI is a kind of protein superstructure called an amyloid.

Chemistry professor Jerry Yang's group at UC San Diego developed non-stick coatings for amyloids as a potential treatment for Alzheimer's disease in 2006. Their idea was to minimize damage by preventing amyloid proteins from interacting with other molecules in the brain.

When this new amyloid, SEVI, was discovered in 2007, Yang was interested in testing whether the coating strategy might interfere with SEVI's role in promoting HIV infection.

Yang's group teamed up with researchers led by Stephen Dewhurst, chair of the microbiology and immunology department at the University of Rochester Medical Center, who studies HIV.

"We tested one of our molecules out on SEVI and found it was able to stop SEVI-enhanced infection of HIV in cells," Yang said. "It works in semen too. Something in semen enhances viral infection - SEVI and maybe other things. This molecule stops that."

When the researchers added the molecule that forms non-stick coatings to a mix of SEVI, virus and cells, rates of infection dropped to levels observed when SEVI was absent. They saw a similar effect with semen as well, evidence that this potential microbicide supplement works to inhibit infection within a mixture of proteins and other molecules found in seminal fluid.

The coating molecule is a modified form of thioflavin-T, a dye that stains amyloid proteins. It fits in between the individual small proteins that cluster to form SEVI and blocks SEVI's interactions with both the virus and the target immune cells.

"Other people have tried to do the same thing by targeting the virus or the cells it infects. What we do is target the mediator between the virus and the cells," Yang said. "By neutralizing SEVI, we prevent at least one way for HIV to attach to the cells."

The new molecule has another advantage. Unlike many current microbicide candidates aimed at reducing HIV infection, this one doesn't cause inflammation in cervical cells.

"I think this will be useful," Yang said, even if it isn't used alone. "Minimally, I think it could be a supplement to microbicide formulations. Our hope is that we can somehow stop this kind of viral transmission."

The National Institutes of Health and the National Science Foundation funded this work. Additional co-authors include Joanna Olsen, Caitlin Brown, Todd Doran, Rajesh Srivastava, Changyong Feng and Bradley Nilsson of the University of Rochester, and Christina Capule and Mark Rubinshtein of the University of California, San Diego.

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